



# A STUDY OF DIABETIC FOOT ULCER AND ITS CORRELATION WITH NEUROPATHY, PERIPHERAL VASCULAR DISEASE AND GLYCEMIC CONTROL

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## ABSTRACT

Diabetes is one of the endocrine disorders that reached epidemic proportions worldwide. The metabolic deregulation associated with diabetes mellitus (DM) causes secondary path physiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes. Diabetic foot ulcer is becoming major concern of diabetic patients. The vascular insufficiency and neuropathy accompanying the diabetic foot most often necessitate amputation of the limb. With the above considerations we undertook the study of 50 patients of diabetic foot admitted in our institute over a period of 2 years and 6 months. The mean age of study subjects was  $53.18 \pm 12.89$  years. Male predominance was observed in study subjects with male to female ratio of approximately 5:1. 52% had BMI above 30. Clinical examination of ulcers for grading revealed that the percentage of grade IV lesion was highest (44%) followed by grades III (24%). Maximum diabetic foot ulcers patients had duration between 8-12 years. 36% of diabetic foot ulcer patients had HbA1c between 8.6-9.5%. There is strong correlation between various grades of diabetic foot ulcers and peripheral neuropathy. Males (76%) had higher signs and symptoms of peripheral neuropathy as compared to females (24%). The most common clinical presentation of peripheral neuropathy was intermittent claudication (28%), paresthesia (26%) and numbness. Our study also identified some important risk factors for diabetic foot ulcers including older age, long duration of diabetes, lack of awareness of this disease, poor glycemic control and rural residence of patients. Sensory neuropathy was also found to be important risk factors for diabetic foot complications.

**KEYWORDS:** diabetic foot, peripheral neuropathy, ulcer, diabetes mellitus, peripheral vascular disease.

## INTRODUCTION:

Diabetes, once considered as a disease of developed countries, is one of the endocrine disorders that reached epidemic proportions worldwide now<sup>[1]</sup>. The metabolic deregulation associated with diabetes mellitus (DM) causes secondary path physiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system<sup>[2]</sup>. Overall all 15% of individuals with diabetes mellitus will have foot ulcer during their lifetime and the annual incidence is 2-3%<sup>[3]</sup>. Diabetic foot ulcer is becoming major concern of diabetic patients and those who treat them from quality of life, social and economical stand point. Diabetic foot is a frequent complication involving the foot of diabetic patient. The vascular insufficiency and neuropathy accompanying the diabetic foot most often necessitate amputation of the limb.

With the above considerations we undertook the study of 50 patients of diabetic foot admitted in our institute over a period of 2 years and 6 months. An emphasis was laid on determination of neuropathy and vascular status and to study in detail the risk factors responsible for development of diabetic foot ulcers and subsequent lower extremity amputation in patients of diabetic foot.

## AIMS AND OBJECTIVES:

- To study risk factors in development of diabetic foot ulcers.
- To study the correlation of diabetic foot ulcer with HbA1c and glycemic control
- To study the incidence of neuropathy and peripheral vascular disease in patients of diabetic foot ulcers.
- To study the outcome of diabetic foot ulcers with available treatment in a tertiary care hospital.

## MATERIALS AND METHODOLOGY:

A cross-sectional descriptive hospital based study consisting of 50 consecutive adults diagnosed with diabetes having diabetic foot ulcer at Diabetes Specialty Clinic in MGM Hospital, Kamothe, Navi Mumbai for a period of 2 Years (Oct 2013 to Nov 2015).

Adults of age more than 18 years diagnosed with DM (according to WHO criteria) and having diabetic foot ulcer of Wagner grade 1 to 4 were included in this study.

Patients with age less than 18, gestational DM, venous ulcers, previous major amputations due to diabetic foot disease or those with Wagner grade 5 diabetic foot ulcer (i.e. gangrene of whole foot) were excluded from the study.

Institutional ethical clearance was obtained. Informed written consent was obtained from all patients enrolled in the study. History and clinical features of all

the patients were recorded in detail. Detailed examination of the involved foot was conducted in all patients to determine the nature of lesion, sensory and motor system involvement and vascularity of the limb (details recorded on pre-designed proforma).

A foot deformity assessment was done which included 1. Small muscle wasting, 2. Hammer or claw toes, 3. Bony prominence, 4. Prominent metatarsal heads, 5. Charcot arthropathy and 6. Limited joint mobility.

Femoral, popliteal, dorsalis pedis and posterior tibial pulses were palpated on both sides to assess peripheral arterial status of all the patients. Presence of 2 or fewer than 4 pulses either with or without pedal edema indicated a peripheral arterial disease, which was further assessed by Ankle-Brachial Index and values < 1.0 were considered as having Peripheral Vascular Disease. Other investigations like fasting blood sugar, hba1c, lipid profile were also done. Vibration sense and hot, cold sensations were tested in all patients by biothesiometry.

## RESULTS:

In our study, the Mean age of study subjects was  $53.18 \pm 12.89$  years and male predominance was observed in study subjects with prevalence of male to female as approximately 5.25:1. Most of the study population were farmers (54%) followed by housewife (12%) and businessmen (12%). 66% of study population had history of trauma and showing 35% increased LDL, 24% Hypertriglyceridemia, 16% Hypercholesterolemia. 68% of diabetic foot ulcer patients had history of smoking. Although smoking provided a higher risk for PVD and to diabetic foot ulcers this did not reach statistical significance in our study. Femoral artery pulsations were present in all patients, popliteal artery pulsation (88%), Posterior tibial (44%), Dorsalis pedis (36%). Deformity was seen in diabetic ulcer patients, amongst them most common was limited joint mobility (8%) & Charcot arthropathy (8%). Critical examination of ulcers for grading revealed that the percentage of grade IV lesion was highest (44%) followed by grades III (24%). [Figure 1]

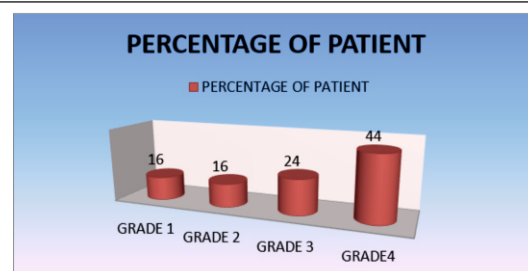


Figure 1: Distribution of Patients According to Grades of Ulcer

Twenty-eight percent of ulcer patients had duration of diabetes between 8.1 to 12, followed by 24% having in duration of diabetes between 4.1 to 8 and 12.1 to 16. The mean duration of diabetes was 11.2.

When grade of diabetic foot ulcers were compared with duration of diabetes, it was found that out of 22 cases of grade 4 diabetic foot ulcer, 7 were having duration between 12.1-16 years and 5 between 16.1-20, while in grade 3 ulcer, 7 were having duration between 8.1-12 years and 5 between 12.1-16. Maximum diabetic foot ulcers patients had duration between 8.1-12 years. [Figure 2]

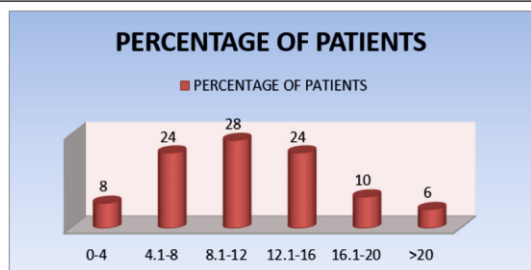


Figure 2: Distribution According to Duration of Diabetes

In the present study, 36 % of ulcer had HbA1c between 8.6 -9.5, followed by 20% in HbA1C between 9.6 -10.5. There is strong evidence of relationship between various grade of diabetic foot ulcers and HbA1C. [Figure 3]

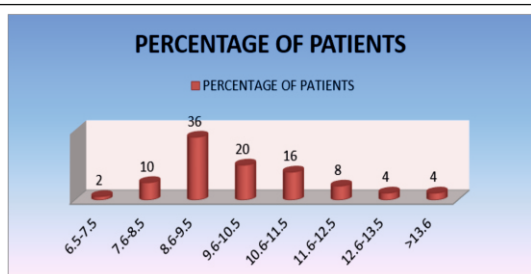


Figure 3: Distribution According to HbA1c

When grade of diabetic foot ulcers were categorized with HbA1C levels, it was found that out of 22 cases of grade 4 diabetic foot ulcer, 8 were having HbA1c between 10.6-11.5 and 6 between 9.6-10.5, while in grade 3 ulcer, 8 were having HbA1c between 8.6-9.5 and 4 between 9.6-10.5. Maximum diabetic foot ulcers patients had HbA1c between 8.6-9.5.

Males (76%) had higher sign and symptoms of peripheral neuropathy as compared to females (24%). The most common clinical presentation of peripheral neuropathy was Intermittent claudication 14 (28%), Parasthesia 13 (26%) Numbness 11 (22%).

33.33%, 28.28% and 22.22% of grade IV, III and II ulcer had peripheral neuropathy. There is strong relationship between various grade of diabetic foot ulcers and peripheral neuropathy (p value 0.001).

In this study, it was observed that 22.72% of diabetic ulcer patients with peripheral neuropathy had HbA1c between 9.6- 10.5 followed by 20.45% having HbA1c between 10.6-11.5.

In this study, it was observed that 25% of diabetic ulcer patients with peripheral artery disease had HbA1c between 10.6 -11.5 followed by 22.22% having HbA1c between 9.6- 10.5.

38.88% patients of stage 2 Peripheral artery disease (PAD) had Ankle Brachial Index (ABI) values 0.50 TO 0.80, and 25 % of STAGE 3-Chronic Critical Ischemia had values 0.30 TO 0.50. No relationship could be established between various grade of diabetic foot ulcers and PAD (p value – 0.198) in our study.

## DISCUSSION:

As per the demographic data obtained from patients of diabetic foot ulcers the mean age of study subjects was 53.18 ± 12.89 years. Male predominance was observed in study subjects with male to female ratio of approximately 5:1. The above trend is reported similar in other studies. All patients had ulcers graded 3–5 in the Wagner classification. The majority of subjects had type 2 Diabetes. Similar finding have been reported by other studies<sup>[4]</sup>. In the present study, 52% had BMI above 30 which is similar to other studies<sup>[5,6]</sup>. In present study Occupation of most of the patients was farming (54%), which is consistent with findings of other studies<sup>[6]</sup>. These findings may be attributed to scant knowledge of the disease and lack of care required to manage the disease and its complications, style of living in the villages and participation in farming and agricultural works and

bare foot walking could be the reason for affecting this group of population the most.

In present study, 66% of study population had a history of trauma. In diabetes mellitus, trauma to the foot plays a critical role in the evaluation of the disease process. In a study done by Kunal Solanki et al<sup>[7]</sup>, (54%) patients gave a history of trauma to foot. In this study 68 % of diabetic foot ulcer patients had a history of smoking. Smoking is an independent risk factor for increased risk of amputation in diabetic patients<sup>[8-10]</sup>. Viswanathan<sup>[11]</sup> found that smoking increases the risk of DFU by reducing blood circulation in the legs and reducing sensation in the feet. The percentage of grade III and IV ulcers was higher in subjects habitual of smoking. Apart from PVD, most probably uncontrolled glucose level also delays wound healing and results in severity of ulcers<sup>[4]</sup>.

Studies have shown, that duration of diabetes, impaired pain perception, absent dorsalis pedis, and the presence of any retinopathy were significant predictors of the presence of foot ulcers<sup>[11]</sup>. In the present study femoral artery pulsations were present in all patients, popliteal artery pulsation (88%), Posterior tibial (44%) and Dorsalis pedis (36%). Several other studies have reported that foot deformities are important contributory risk factors by predisposing skin to high pressure at the site of the foot deformity<sup>[12,13]</sup>. In this study, most common was deformity was limited joint mobility (8%) & Charcoat arthropathy (8 %). In a similar study done by Khalid Mahmood et al.<sup>[5,14]</sup> patients had significant foot deformity.

In the present study, Clinical examination of ulcers for grading revealed that the percentage of grade IV lesion was highest (44 %) followed by grades III (24%). Similar findings were observed by others 81 in which the majority of ulcer was of grade IV. Maximum diabetic foot ulcers patients had duration between 8 - 12 years which is consistent with other studies<sup>[14]</sup>. More commonly, long duration and poor metabolic control of diabetes are thought to be factors that increase the risk of chronic complications<sup>[82]</sup>. There is strong evidence of relationship between various grades of diabetic foot ulcers and HbA1C. In present study, 36 % of diabetic foot ulcer patients had HbA1c between 8.6 -9.5%. In another study, 90.52% patients had HbA1c level more than 8%<sup>[14]</sup>. It is clear that those patients, with high HbA1c levels have developed more severe grades of diabetic foot ulcers, reflecting that poor glycaemic control is also an important contributing factor.

There is strong Correlation between various grade of diabetic foot ulcers and peripheral neuropathy. In the present study, males (76%) had higher signs and symptoms of peripheral neuropathy as compared to females (24%). The most common clinical presentation of peripheral neuropathy was intermittent claudication (28%), paresthesia (26%) and numbness. In another similar study, (84.4%) patients had moderate to severe neuropathy<sup>[10]</sup>. Also in other study, there were more than 75% of subjects with peripheral neuropathy<sup>[4]</sup>. In a study done by Mohammad Zubair et al<sup>[11]</sup>, neuropathy was observed in 50.6% of patients in diabetic foot ulcer patients.

The pathogenesis of diabetic neuropathy includes various factors, like hyperglycemia, Vaso Nervorum, Protein Kinase C pathway activation, abnormal fatty acid metabolism, Myo-inositol, advanced glycated end product, antibody to neural tissue<sup>[16-18]</sup>. In the year 2004, four major pathogenic pathways mechanism explaining the hyperglycaemic nerve damage were explained in a paper by Brownlee M et al<sup>[19]</sup>. These four major mechanisms are increased intracellular formation of AGEs, increased polyol pathway, activation of protein kinase C and increased homosamine pathway flux. These are now accepted as major mechanisms for causation of Peripheral neuropathy. In the present study, it was observed that 25% of diabetic ulcer patients with peripheral artery disease. There was no relationship between various grades of diabetic foot ulcers and PAD (p value – 0.198).

## CONCLUSION:

Our study confirmed the high prevalence of foot ulcers amongst uncontrolled diabetic patients.

The study also identified some important risk factors for diabetic foot ulcers including older age, long duration of diabetes, lack of awareness of this disease, poor glycemic control and rural residence of patients which was consistent with other studies conducted by Rao PV, Ushabala P, Seshiah V, et al and Ramachandran A, Snehalatha C, Kapur A, et al.<sup>[20,21]</sup>. Sensory neuropathy was also found to be important risk factors for diabetic foot complications. It is felt that knowledge of the risk factors is of paramount importance for early and better management of diabetic foot ulcers. There is a need to educate create awareness about diabetes and its complications, especially amongst rural populations.

In the primary care setting, diabetic patients should be screened for foot ulcers annually, with higher-risk patients screened more frequently. The annual foot exam should include visual inspection of the feet for calluses, skin integrity, and bony deformities. Patients with ulcerations or gross deformities should be referred to a podiatrist or General surgeon depending on available resources. The foot exam should also include screening for loss of protective sensation with the Semmes-Weinstein monofilament. Inability to perceive the 10-gram load imparted by the filament is associated with large-fiber neuropathy and a 7-fold increase in the risk of ulceration.

In addition, diabetic patients should be screened for peripheral vascular disease through palpation of the dorsalis pedis and posterior tibialis pulses and measurement of ankle-brachial index. Patients with peripheral vascular disease should be given additional counseling on smoking cessation, as smoking worsens peripheral artery disease, and referral to a vascular surgeon should be considered in case significant PVD is diagnosed.

All diabetic patients, especially those who have impaired monofilament sensation, should be educated about foot precautions, including daily inspection of the toes and feet, wearing well-fitting socks and shoes, and keeping the skin clean and moist.

**Conflict of Interest:** None.

#### REFERENCES:

1. Wild S, Roglic G, Green A, Sicree R, King H (2004) Global prevalence of Diabetes : estimates for the year 2000 and projections for 2030. *Diabetes Care* 27: 1047-1053.
2. International Diabetes Federation (2012) The Global Burden. IDF Diabetes Atlas Fifth Edition.
3. Amos AF, McCarty DJ, Zimmet P, The rising global burden of diabetes and its complications: estimates and projections to the year 2010, *Diabet Med* 1997; 14 (5) S1-S85.
4. Shailesh K. Shahi, ; Surya K Singh, ; Sushil Kumar- Prevalence of Diabetic Foot Ulcer and Associated Risk Factors in Diabetic Patients From North India. *The Journal of Diabetic Foot Complications*, 2012; Volume 4, Issue 3, No. 4, Pages 83-91.
5. Ravishankar Gadepalli- A Clinico-microbiological Study of Diabetic Foot Ulcers in an Indian Tertiary Care Hospital care. [diabetesjournals.org/content/29/8/1727](http://diabetesjournals.org/content/29/8/1727).
6. Nasser Janmohammadi, Mohammad Reza Hasanjani Roshan, Management of diabetic foot ulcer in Babol, North of Iran: an experience on 520 cases. *Caspian J Intern Med*. 2012 Summer; 3(3): 456-459.
7. Dr. Kunal Solanki, Dr. Hiren Parmar- The Surgical Management of Diabetic Foot. *NJIRM* 2010; Vol. 1(4).Oct- Dec.
8. Moss SE, Klein R, Klein BE. The 14-year incidence of lower extremity amputations in a diabetic population. The Wisconsin Epidemiolog Study of Diabetic Retinopathy. *Diabetes Care* 1999; 22(6):951-959.
9. Adler AI, Boyko EJ, Ahroni J, Smith DG. Lower extremity amputation in diabetes: the independent effects of peripheral vascular disease, sensory neuropathy, and foot ulcers. *Diabetes Care* 1999; 22:1029-1035.
10. Mayfield JA, Reiber GE, Nelson RG, et al. A foot risk classification system to predict diabetic amputation in Pima Indians. *Diabetes Care* 1996; 19(7):704-709.
11. Viswanathan V. The diabetic foot: perspectives from Chennai, South India. *Int Low extrem Wounds* 2007; 6: 34-6.
12. Reiber GE, Vileikyte L, Boyko EJ, del Aguila M, Smith DG, Lavery LA, et al. Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. *Diabetes Care* 1999; 22:157-62.
13. De Sonnaville JJ, Colly LP, Wijkkel D, Heine RJ. The prevalence and determinants of foot ulceration in type II diabetic patients in a primary health care setting. *Diabetes Res Clin Pract* 1997; 35: 149-56.
14. Khalid Mahmood, S. Tehseen Akhtar- Clinical Profile and Management Outcome of Diabetic Foot Ulcers in a Tertiary Care Hospital. *Journal of the College of Physicians and Surgeons Pakistan* 2008, Vol. 18 (7): 408-412
15. Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. *Diabetes Care* 2006; 29: 1288-1293.
16. Polydefkis M, Griffin JW, McArthur J. New insights into diabetic polyneuropathy. *JAMA* 2003; 290(10):1371-1376.
17. Haslbeck KM, Schleicher E, Bierhaus A et al. The AGE/RAGE/NF-(kappa) B pathway may contribute to the pathogenesis of polyneuropathy in impaired glucose tolerance (IGT). *Exp Clin Endocrinol Diabetes* 2005; 113(5):288-291.
18. Cameron NE, Cotter MA. Metabolic and vascular factors in the pathogenesis of diabetic neuropathy. *Diabetes* 1997; 46(suppl 2):S31-S37.
19. Brownlee M. Biochemistry and Molecular cell biology of diabetic complications. *Nature*. 2001; 414: 813-820
20. Rao PV, Ushabala P, Seshiah V, et al. The Eluru survey: prevalence of known diabetes in a rural Indian population. *Diabetes Res Clin Pract* 1989; 7 :29-31.
21. Ramachandran A, Snehalatha C, Kapur A, et al. Diabetes Epidemiology Study Group in India (DESI). High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. *Diabetologia* 2001; 44 :1094-101.